included with respect to now independent claim 3. No new matter has been added by these amendments. Reconsideration is respectfully requested in light of these amendments and the following remarks.

I. Rejection of Claims Under 35 U.S.C. 112, Second Paragraph

Claim 10 has been rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 10 has been amended to correct the antecedent basis. Withdrawal of this rejection is respectfully requested.

II. Rejection of Claims Under 35 U.S.C. 102

Claims 1, 2 and 14 were rejected under 35 U.S.C. 102(b) as being anticipated by Leesoon-Wood (1996). The Examiner suggests that this abstract discloses inhibition of C3H 10T1/2 cells via administration of 15 mer antisense oligonucleotides targeted to iNOS mRNA. Applicants respectfully traverse this rejection.

At the outset, Applicants have amended the claims to refer to targeting of specific regions of two specific human iNOS RNA sequences with antisense compounds. These two sequences, SEQ ID NO's: 3 and 17 are taught in the specification as filed and referred

to specifically at page 78. The regions now claimed also are taught in the specification as filed at Examples 15 and 16.

Leesoon-Wood et al. (1996) is an abstract only with very little detail provided. The abstract discloses the preparation of 6 antisense oligonucleotides, 15 mer each, that corresponded to different parts of the coding region of an iNOS. However, the exact sequence of this iNOS and the target regions within the coding region of this iNOS are not taught or suggested. In addition, no other target sites on the gene are taught or suggested. Therefore, this paper fails to teach the regions recited in the amended claims and cannot anticipate the instant invention as claimed. Accordingly, withdrawal of this rejection is respectfully requested.

Claims 1, 2, 4, 5 and 14 were rejected under 35 U.S.C. 102(b) as being anticipated by Peresleni et al. (1996). The Examiner suggests that this paper discloses phosphorothioate antisense compounds targeted to the 5'-UTR, initiation codon region of human iNOS mRNA as well as inhibition of human iNOS in kidney tubular cells. Applicants respectfully traverse this rejection.

As discussed supra, Applicants have amended the claims to refer to specific target regions of two specific human iNOS sequences. Peresleni et al. teach only antisense compounds targeted to [illegible] of human iNOS cDNA that is [illegible] by GenBank

accession number L24553 (see page F972). The authors claim this region of that sequence corresponds to the 5'-UTR, the initiation codon, and two codons from the open-reading frame of iNOS cDNA. No other target regions of the gene are taught or suggested. Since the present invention teaches antisense targeted to two other iNOS sequences (SEQ ID NO's: 3 and 17, which correspond to two different GenBank accession numbers, L09210 and L07868, respectively, this paper fails to teach the regions recited in the amended claims and cannot anticipate the instant invention. Accordingly, withdrawal of this rejection is respectfully requested.

Claims 1, 2, 4, 5, 11, 13 and 14 were rejected under 35 U.S.C. 102(b) as being anticipated by Ding et al. (1996). The Examiner suggests that Ding et al. disclose a 21 mer phosphorothioate antisense oligonucleotide targeted to bases 1-21 of murine iNOS mRNA as well as administration of this oligonucleotide to mice as a model for multiple sclerosis. Applicants respectfully traverse this rejection.

As discussed supra, Applicants have amended the claims to refer to specific target regions of human iNOS of SEQ ID NO's: 3 and 17. Ding et al. teach only one antisense compound targeted to bases 1-21 of the translation initiation site of mouse iNOS mRNA. No other

to teach either targeting of human iNOS, as now claimed, as well as the regions recited in the amended claims. Therefore, this reference cannot anticipate the instant invention as claimed. Accordingly, withdrawal of this rejection is respectfully requested.

III. Rejection of Claims Under 35 U.S.C. 103(a)

Claims 6-10 and 12 were rejected under 35 U.S.C. 103(a) as being unpatentable over Ding et al., Peresleni et al., and Leesoon-Wood et al., in view of Monia et al. (US Patent 5,872,242). The Examiner suggests it would have been *prima facie* obvious for one of skill to make and use antisense compounds to iNOS RNA based on the teachings of Ding et al., Peresleni et al., and Leesoon-Wood et al., as relied upon above, and further because these references teach implication of iNOS in pathological conditions and the benefits of inhibiting expression of iNOS, while Monia et al. teach modifications of antisense as claimed. Applicants respectfully traverse this rejection.

At the outset, as discussed supra in Section II, the base claims from which claims 6-10 and 12 depend have been amended to refer to specific target regions of two specific human iNOS sequences that are not taught by any of the primary references cited by the

Peresleni et al., Leesoon-Wood et al.) fail to teach the limitations of the claims as amended.

The secondary reference of Monia et al. teaches modifications of antisense oligonucleotides in general. However, nowhere does this patent teach or suggest antisense compounds of any type targeted to any region of the human iNOS RNA. Therefore, this secondary reference fails to overcome the deficiencies in teaching of the primary references.

To establish a *prima facie* case of obviousness, three basic criteria must be met. MPEP 2143. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art must teach or suggest all claim limitations. Clearly, the combination of prior art cited fails to teach or suggest the limitations of the claims as amended, which claim antisense compounds targeted to specific regions of iNOS RNA, and thus cannot render the instant claimed invention obvious. Therefore, this combination of prior art cannot render the instant invention obvious. Withdrawal of this rejection is therefore respectfully requested.

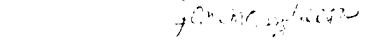
IV. Objection to Claim 3

Claim 3 was objected to as being dependent upon a rejected base claim but the Examiner suggests it would be allowable if rewritten in independent form. Applicants have amended this claim to be independent as suggested by the Examiner. Withdrawal of this objection is respectfully requested.

V. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,



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